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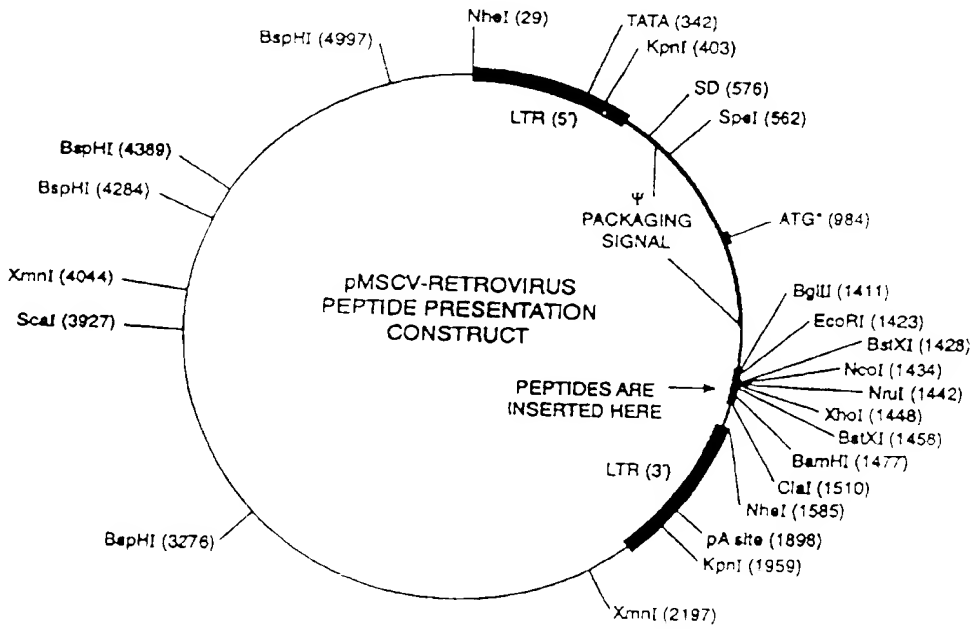
(54) Title: METHODS FOR SCREENING FOR TRANSDOMINANT INTRACELLULAR EFFECTOR PEPTIDES AND RN MOLECULES



(57) Abstract

Methods and compositions for screening for intracellular transdominant effector peptides and RNA molecules selected inside livin cells from randomized pools are provided.

CLAIMS

I claim:

1. A method for screening for a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:
a) introducing a molecular library of randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence;
b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent.

2 A method according to claim 1 further comprising the step:
c) isolating said cell exhibiting an altered phenotype.

3 A method according to claim 2 further comprising the step:
d) isolating a candidate nucleic acid from said cell.

4. A method according to claim 2 or 3 further comprising the step:
e) isolating a target molecule using
i) a candidate nucleic acid; or
ii) the expression product of a candidate nucleic acid.

5. A method according to claim 1 wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized candidate expression products.

6. A method according to claim 5 wherein said randomized candidate expression products are peptides.

7. A method according to claim 5 wherein said randomized candidate expression products are nucleic acid transcripts.

8. A method according to claim 1 wherein said nucleic acids further comprise a presentation sequence capable of presenting said expression product in a conformationally restricted form.

9. A method according to claim 1 wherein said introducing is with retroviral vectors.

10. A method according to claim 1 wherein said cells are mammalian cells.

11. A method according to claim 1 wherein said library comprises at least 10^4 different nucleic acids.

12. A method according to claim 1 wherein said library comprises at least 10^5 different nucleic acids.

13. A method according to claim 1 wherein said library comprises at least 10^6 different nucleic acids.

14. A method according to claim 1 wherein said library comprises at least 10^7 different nucleic acids.

15. A method according to claim 1 wherein said library comprises at least 10^8 different nucleic acids.

16. A molecular library of retroviruses comprising at least 10^4 different randomized nucleic acids.

17. A molecular library of retroviruses according to claim 21 comprising at least 10^5 different randomized nucleic acids.

18. A molecular library of retroviruses according to claim 21 comprising at least 10^6 different randomized nucleic acids.

19. A molecular library of retroviruses according to claim 21 comprising at least 10^7 different randomized nucleic acids.

20. A molecular library of retroviruses according to claim 21 comprising at least 10^8 different randomized nucleic acids.

21. A cellular library of mammalian cells containing a molecular library of retroviral constructs, said molecular library comprising at least 10^4 different randomized nucleic acids.

22. A cellular library according to claim 26 wherein said constructs are integrated into the cellular genome.